

# Are you ready for Data Sharing?

---

## Lessons Learned from the Fernald Community Cohort

**A Large Database and Biobank with a 20 Year Heritage**



Susan M. Pinney, PhD  
February 6, 2012

University of Cincinnati, Dept. of Environmental Health

# U.S. Department of Energy Uranium Processing Plant at Fernald, Ohio

- Known as the Feed Materials Production Center (FMPC, 1952-1989)
- Processed uranium ore and recycled materials to make highly refined uranium metal products used in DOE nuclear weapons production complex
- Chemical separation: uranyl nitrate,  $UO_3$ ,  $UF_4$ ,  $UF_6$



# Fernald Medical Monitoring Program (FMMP)

**Medical Monitoring Program established as a result of a litigation settlement**

During the period from 1990 to 2008, the FMMP provided periodic medical examinations for persons who lived within a five mile radius of FMPC for at least a two year interval between 1952 and 1984. FMPC workers have a separate monitoring program.

|       | Male | Female |             |
|-------|------|--------|-------------|
| Adult | 3967 | 4821   | 8788        |
| Child | 521  | 473    | 994         |
|       | 4488 | 5294   | <b>9782</b> |

# FMMP Adult Examinations

## Yearly Questionnaire:

Health history; Smoking and alcohol use; Medications; Family history; Residence (address) history; Occupational, hobby, and exposure history; Detailed reproductive history; Contact persons; SF-36 health perception.

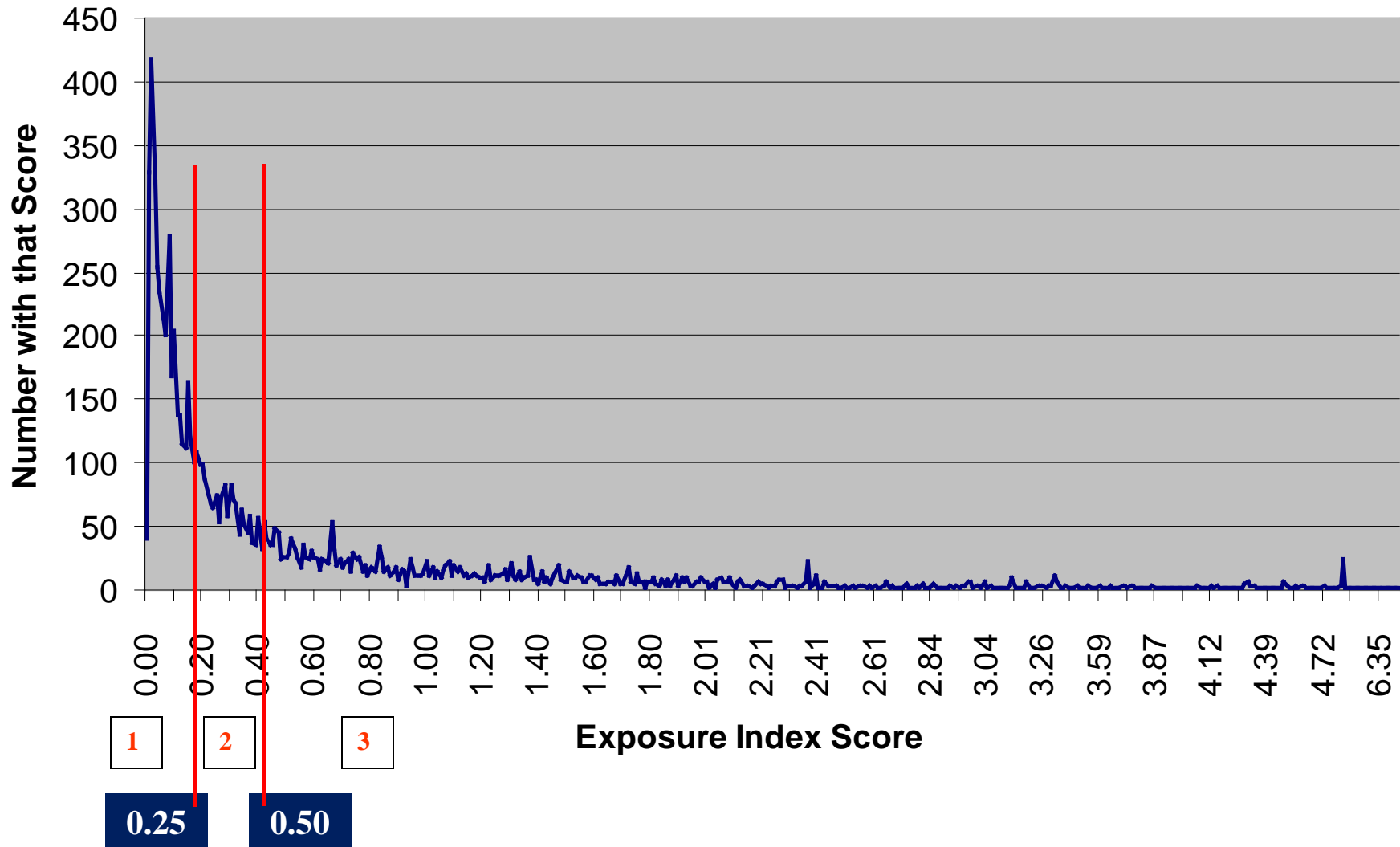
## Physician Examination every 2 to 3 years:

Health history; Review of Systems; Medications; Social history; Comprehensive physical examination; laboratory tests; mammograms

**Blood and urine obtained at time of first exam and frozen for later use.  
(Serum, Plasma, Whole blood, Urine [buffered and non-buffered])**



# Distribution of Frequency of Exposure Index Scores



# Fernald Medical Monitoring Program becomes the Fernald Community Cohort

---

- January 13, 2010. Agreement between the Fernald Citizens' class and the University of Cincinnati transfers custodianship of the FMMP research resources to the University of Cincinnati.
- UC College of Medicine, Department of Environmental Health assumes responsibility for the **Fernald Community Cohort**.

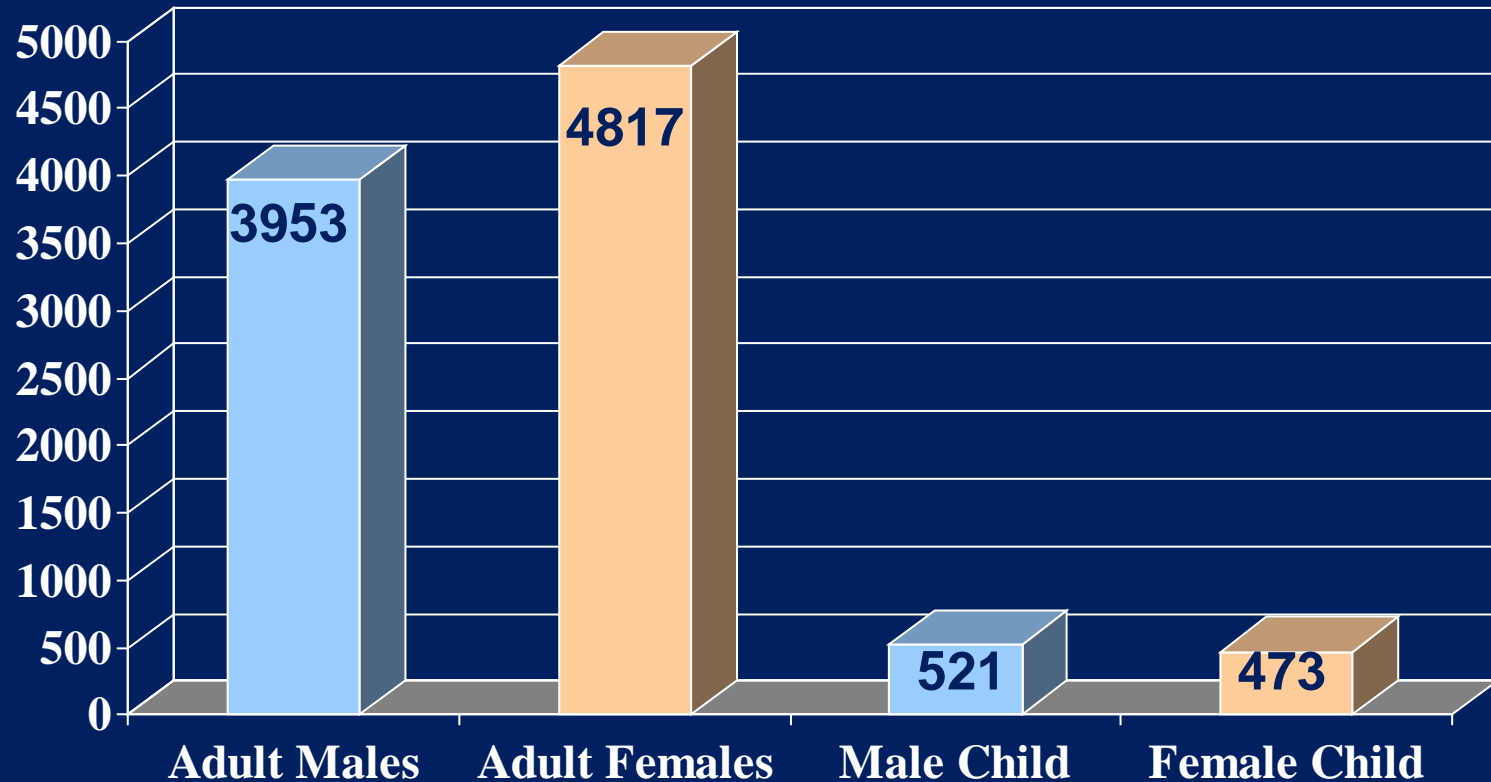
# Research Resources

**What's available in the Fernald Community Cohort  
database and biospecimen repository?**



# Fernald Community Cohort Members

## N=9782





# Medical Condition Information

## FMMP Physical examination

Digital images of mammograms (future, chest X-rays)

## Outside medical records including:

- ◆ Death certificates
  - ◆ Pathology reports
  - ◆ Medical test reports
  - ◆ Operative and discharge summaries.
- 
- Exam findings coded with study-specific codes (physical exam, EKG, chest x-rays, PFTs, mammograms, etc.)
  - Diagnoses coded with ICD-9 codes
  - All information stored in SAS files and digital images.



## **Examinations: Whole Blood, Serum, Plasma and Urine Samples for future studies**

- At the first examination, three 1 ml aliquots of samples of various media were obtained.
  - ◆ Serum
  - ◆ Plasma
  - ◆ Whole blood
  - ◆ Urine
  - ◆ Urine with buffer – to maintain pH at 7.5
  - ◆ 15 aliquots per person- for future analyses
- **At later exams**, serum and plasma were obtained on some participants.
- In 2006-2008, additional whole blood and serum obtained on all participants who came for an exam.
- **Over 160,000 samples in five freezers.**

# Value of the Archived Data

- Large volume of data on persons from whom samples were collected.
  - ◆ Data has been coded by certified medical record coders and in SAS data files.
  - ◆ Medical record verification of cancer diagnoses.
  - ◆ Can be used for risk factor characterization over time (including exposure factors) and disease.
  - ◆ Can be used to create tailored comparison groups for genetic and proteomic studies (e.g. “highly resistant” to cancer persons with 80 pack year smoking history and at least 60 years old with no family history of lung cancer.)

# Value of the Archived Samples

- Very large cohort: Over 160,000 samples on over 9000 persons.
- Prospective Cohort:
  - ◆ Samples collected early in the Program, with many years of follow-up; can be used to identify genetic and proteomic predictors of disease.
  - ◆ Whole blood, serum and urine samples can be used to identify biomarkers of previous metal and chemical exposures prior to disease
  - ◆ Very few resources of archived samples, with 15+ years of follow-up, exist.
  - ◆ (genomic data – require that it is shared with FCC; won't discuss otherwise)

# Success – but a BIG Challenge!

- **Over 50 studies have been approved**, conducted by researchers from UC, the National Cancer Institute, and the University of South Carolina. Currently UC is collaborating with the University of Vermont on developing a large study of biomarkers and early effects of exposure to radiation.
- **46 publications in scientific journals** have resulted from these studies.
- **BUT, when we started in 1990, not even thinking about data sharing**
  - Not a usual practice
  - IDs (types of data, samples) – practices have changed
  - Big concerns about confidentiality of data
  - Specialized software not available
  - Resources for data sharing not in the budget

# Access to Data and Biospecimens

“Applying the precautionary principle”

- **Any qualified researcher may apply to use the data and biospecimens for research.** Application is online at FCC website. Research question, specific aims, study design, types of data
- Applications for **access to the data and biospecimens** are reviewed and approved by an **Advisory Committee**.
- Data files of de-identified data (no DOB or DOD), prepared for needs specific to investigators. Most data only analyses do not require separate IRB approval.
- Biospecimens provided to researchers after they obtain IRB approval for their studies.
- No follow-back – collection of additional data or biospecimens from FMMP cohort.



# Fernald Community Cohort Advisory Committee

Serve as delegates for study participants



# Learning:

## Consent requirements change over time

- In 1990 consent requirements were minimal.
- Be proactive about keeping your IRB informed.
- Reconsent is very difficult if you have not kept in contact.

12/14/91

### FERNALD MEDICAL MONITORING PROGRAM

#### CONSENT TO PARTICIPATE

The Fernald Medical Monitoring Program is designed to provide you a free, comprehensive evaluation of your current health and risks for future disease. The program is entirely voluntary. We hope that you will take advantage of all the examinations and tests offered you. However, you are free to refuse any part or all of the program, the procedures we will follow, the type of information you will receive, potential risks of the testing, and the measures we have taken to preserve confidentiality.



# 1991 FMMP Consent Form

- 4) **Laboratory Tests** - Blood and urine samples will be obtained for a series of screening tests which will include blood counts, blood salts, liver and kidney function tests, a blood sugar, and an urinalysis. Two samples of blood will be obtained and frozen for future additional testing if necessary. Your blood will not be tested for HIV antibodies (AIDS test).

separately. No one is to have access to any of this information except as authorized by the Fernald Settlement Fund Trustees. If authorized by the Settlement Fund Trustees, scientific data or medical information may be analyzed and presented in court, at scientific meetings, or in professional

journals so that the overall results of this Program may be useful to others. However, no presentation or report shall include your name or any other identifying information which might compromise your right to privacy; and every reasonable effort shall be made to ensure your anonymity.

# Consent in 2007 and thereafter

7. **Blood and urine samples for research** - You are asked to take part in a component of the Fernald Medical Monitoring Program that includes collection of blood and urine samples for use in future research studies. Researchers will use blood and urine samples in conjunction with personal information in FMMP records to study how different components of blood and urine maybe related to disease and how genes, lifestyle, and our environment may lead to disease. We will ask you to donate 3 tubes of blood (about 4-6 teaspoons) that will be drawn from a vein in your arm at the same time as we are taking blood for the usual tests that are part of the FMMP examination. We also ask that you allow us to freeze a portion of your urine sample.

## VI. RESEARCH

### Research Using Data

If authorized by the Fernald Settlement Fund Trustees, scientific data or medical information may be analyzed and presented in court, at scientific meetings, or in professional journals so that the overall results of this Program may be useful to others. However, no presentation of results will include your name or any other identifying information, which might compromise your right to privacy; every reasonable effort shall be made to ensure your anonymity.

Under federal law, researchers who use information about the health of their research participants are required, except in specific circumstances, to get written permission to use their participants' health information for the research study. We are asking for your authorization to allow researchers approved by the Fernald Settlement Fund Trustees to use or disclose certain information about your health. Your information may be used for research studies currently being conducted (attached) or future research studies approved by the Fernald Settlement Fund Trustees.

### Research Using Blood Samples

Your samples will only be released for research purposes to researchers who have been approved by the Fernald Settlement Fund Trustees.

The exact tests that will be performed in future research studies are not known at this time but are likely to include the following: 1) the study of blood proteins; 2) the study of genes and changes in genes that may be involved in hereditary and non-hereditary disease development; and 3) the study of how race/ethnicity, age, lifestyle, the environment, and other factors may play a role in disease development. At no time will your name and address, or any other identifying information,

be given for research purposes without your permission. Instead, requests for use of the information in the study will be handled in the following way.

Researchers who are interested in using blood samples have to complete a research plan with specific information about their study, including a description of how they will use the information. Plans will be reviewed by a group of experienced scientists and the Fernald Trustee, who will judge each plan for its scientific merit, its potential contribution to the prevention or cure of disease, and for the qualifications of the research team. Because we realize that the information and samples you provide are an invaluable contribution to science, their use in any research study will be carefully weighed. If a plan is approved, your information and samples will only be shared by us with an approved researcher after your name and address, and any other identifying information, have been removed and a code number has been given.

If an approved researcher would like to collect more information and/or blood samples, not routinely collected by the research staff, we will contact you to explain the study, and you will have the choice of whether to participate before you would be contacted directly by the researcher.

By signing this consent form you agree to give to the FMMP all rights to the access and control of any obtained blood, urine or tissue. The FMMP may retain, preserve, or dispose of these samples and may use them in future research studies for an unlimited period of time. The results of future studies conducted may be published or presented to scientific groups, but you will not be identified by name in these publications.

# Get Ready: Data Collection

---

- Document, document, document
- Exam protocols (revisit and revise every year, keep yearly protocols)
- Questionnaire QxQs – yearly (yes, it takes much effort)
- Data entry protocols for each form
- Laboratory data – document methods and laboratory reference intervals for each year
- Code, code, code – everything you can! \$

# Plan Ahead: Derived Variables

---

- Standardized derived variables will maintain consistency in analyses (and protect the credibility of your cohort)
  - Standardized application of missing data rules
  - Provide SAS code
  - Also willing to provide source variables
- 
- Smoking pack years (yearly and cumulative); same for alcohol
  - Diet nutrient analysis
  - Exposure metric for uranium – air, water, organ doses; prevents need to distribute geocodes



# Plan Ahead: Family Relationships

---

- Document family relationships within the cohort within the database (data have been collected)
  - Start early so that you can verify with second data collection
  - Select software carefully; \$
- 
- Studies: heritability, family dynamics, risk factors
  - Selected study biospecimens are independent of each other (by blood relation) can be selected – software plus personnel effort

# Get Ready: Data Dictionary

---

- From the start, plan for a well-designed data dictionary
- Takes time and money! \$\$
- Think “outside”, not just “in-house”
- Specialized software – SAS descriptors are not sufficient but better than nothing
- Coded or searchable variables
- Variables linked across years

# Data Dictionary Database

FMMP Data Dictionary Database - [frmMain : Form]

File Edit View Insert Format Records Tools Window Help Adobe PDF Type a question for help

**FMMP DATA DICTIONARY DATABASE**

Search File: DIET Diet Questions

**SAS FILE Variables**

|                          |   |
|--------------------------|---|
| <b>Name</b>              | GRILSUMM  |
| <b>Type</b>              | num   |
| <b>Length</b>            | 8   |
| <b>Format</b>            |   |
| <b>Informat</b>          |   |
| <b>Short Description</b> | Servings of grilled meat per week in summer   |
| <b>Long Description</b>  | During the summer, how many servings of grilled meat, chicken, or fish do you eat per week? |

| Code | Code Description |
|------|------------------|
|------|------------------|

Record: 1 of 1

Record: 8 of 51

Coded Variable Value

NUM



# Getting Ready: Credibility

---

- Demonstrate that the (unexposed) cohort is large enough to provide significant statistical power for genomic and proteomic studies
- Demonstrate the “credibility” of the cohort by producing more peer reviewed publications.
- (Demonstrate that the racial and ethnic homogeneity of the population is an advantage)
- (Demonstrate that a significant portion of the population has not had exposure beyond background levels – uranium particulates; radon)

# Learnings: Data Sharing Policy

- Disclosures
- Students or Trainees – ensure supervision by making the faculty member the PI
- IRB approval – or exempt? Need to know for data file preparation
- Meeting or conference call of Advisory Committee?
- Sample size calculation – are sufficient data available for sufficient statistical power?
- Yearly reports; time limitation on manuscript submission and publication
- Standard statement for description of the cohort; check description and grant acknowledgment
- Return or destroy data files – difficulty to ensure compliance. Better to have strong statements re use outside of approval

# Learnings: Costs for Data Sharing

- Data files - \$1200 for basic fee (includes up to 10 hours of consultation with the Research Director or Research Coordinator; 2 hours of effort for preparing data files)
- Additional preparation - \$100 per hour for consultation and \$80 per hour for data manager
- Other cost considerations – additional outside medical records; identification of phenotypes using operational definitions
- Preliminary data for grants – charge?
- Needed to develop a Charge Center so that costs could be charged to grants; indirect costs additional for non-UC/CCHMC investigators
- What about revenue from patents for new predictive biomarkers or imaging procedures?

# Getting Ready: Website

---

- Website will publicize the availability of data and biospecimens; also will reduce investigator time in consultations with investigators
- Description of cohort; questionnaires and other data collection instruments; laboratory methods (including exposure biomarkers)
- Protocols and timelines
- Code sets
- Data dictionary
- Outcome frequencies; exposed person frequencies
- Publications resulting from data sharing
- \$\$\$\$\$\$\$\$ - our website is woefully out of date



# **Learnings:**

## **Biospecimen Inventory**

---

- Inventory database and queries: investment in design pays off
- Redundancy is good (binders and database)
- Keep up with software updates
- Periodic back-ups of computer inventory database.
- QC queries for duplicate records or no records
- Periodic freezer inventories, especially after samples have been moved because of freezer maintenance issues

# **Learnings:**

**Periodic quality assessment of samples are an important component of quality assurance**

---

- Determine long term stability of specimens for future analyses
- Determine DNA quantity and quality for future analyses; inventory database for DNA aliquots and dilutions
- Test the specimen locator system
- Determine future needs and resources for specimen preservation; \$\$\$\$\$\$ for freezer oversight, maintenance contracts, backup systems

# Learnings: Biospecimen Sharing Policy

---

- Sample size application – how many biospecimens are really needed?
- Prioritization of samples of exposed persons
- Should biospecimens be returned?
  - ◆ Serum, plasma and urine; paraffin-fixed tissue
  - ◆ Split aliquots – documentation in inventory
  - ◆ Whole genome amplified DNA?
- Meeting of Advisory Committee
- Sufficient funds? Prevents “squirreling” of biospecimens



# Learnings: Costs for Biospecimen Sharing

---

- Costs
- Basic fee: \$500 for up to 200 samples; \$50 for each 50 additional samples
  - ◆ for preparation work (persons who meet eligibility requirements, locate biospecimens in inventory, select which ones to pull [use of biospecimen, freezer location])
- Additional charge of \$5 per sample (team of 4 persons)
- Charge center and additional indirect cost for “outside” investigators
- A few samples for preliminary data – charge?



## Fernald Medical Monitoring Program The Fernald Community Cohort

Volume 1, Issue 1

June, 2010

Department of Environmental Health, University of Cincinnati

### Records of the Fernald Medical Monitoring Program Now at the University of Cincinnati

#### Special points of interest:

- FMMP Records now at the University of Cincinnati
- UC will develop the FMMP data and biospecimens as a national resource for studies of radiation and uranium exposure
- First meeting of Advisory Committee has been held

#### Fernald Community Cohort Research Office

Phone: 513-558-0487

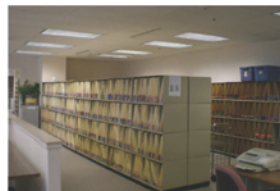
Fax: 513-558-4240

Email: buckhojm@ucmail.uc.edu

#### Inside this issue:

- |  |   |
|--|---|
| Researchers using FMMP data and biospecimens | 2 |
| For women: Your Mammograms                   | 3 |
| Health of those in the FMMP                  | 3 |
| Jenny Buckholz, RN, MSN wins Award           | 3 |
| Medical journal articles describe the FMMP   | 4 |

The University of Cincinnati has recently become the custodian of all the medical charts, x-rays, mammogram films and biospecimens of the Fernald Medical Monitoring Program (FMMP). The records are now stored in a very secure space at the UC Reading Road Campus and the biospecimens are in freezers in a monitored research freezer area of Children's Hospital Medical Center.



X-Ray films of the Fernald Medical Monitoring Program

On January 13, 2010, Judge Spiegel approved a custodianship agreement between the class of community residents and the University of Cincinnati. The Agreement also provides for an Advisory Committee with 10 members from the Fernald area community, and three UC research scientists. The Committee will approve applications for use of the clinical data and biospecimens for future research projects.

Dr. Susan Pinney, the epidemiologist of the cohort, is now

**Fernald Medical Monitoring Program**



**Fernald Community Cohort**

Since the examination program of the FMMP is no longer in operation, we have changed the name to the **Fernald Community Cohort**.

the Research Director of the program, and Dr. Robert Wones, the former Medical Director of the FMMP, is a member of the Advisory Committee. The first meeting of the Advisory Committee was held on Tuesday, April 20.

Ms. Jeanette Buckholz continues to work with the program records at the UC Department of Environmental Health. She can be reached at 513-558-0487.

UC hopes to develop the FMMP

data and biospecimens into a national resource for studies of uranium and radiation exposure, and also other medical studies such as those which will identify biomarkers of high risk of cancer or other diseases. The costs of maintaining the data and biospecimens are currently being shared by the Department of Environmental Health at UC, some remaining funds from the settlement, and the support from the Dean of the UC College of Medicine.

## Acknowledgments

**Raymond Suskind, MD**  
**Robert Wones, MD**

**Shuk-Mei Ho, PhD**

**Jeanette Buckholz, RN**  
**MSN**